

IN THE CLAIMS

1. (withdrawn) A method for preparing a humanized or human chimeric monoclonal antibody, with high effector activity, comprising:

- a) producing and purifying monoclonal antibodies obtained from different sources selected from the group consisting of cells, plants and non-human animals,
- b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies, and
- c) selecting antibodies for which the fucose content/galactose content ratio is less than or equal 0.6.

2. (withdrawn) The method of claim 1, wherein said antibodies are produced in genetically modified cells by introducing at least one vector allowing the expression of said antibodies, said cells being eukaryotic or prokaryotic cells selected from the group consisting of cells from mammals, insects, plants, bacteria and yeasts.

3. (withdrawn) The method of claim 1 wherein said cells are genetically modified by introducing at least one vector allowing the expression of at least one polypeptide having a glycosyl transferase activity.

4. (withdrawn) The method of claim 3, wherein said glycosyl transferase activity is a galactosyl transferase activity.

5. (withdrawn) The method of claim 4, wherein said galactosyl transferase activity is a beta(1,4)-galactosyl transferase activity or a beta(1,3)-galactosyl transferase activity.

6. (withdrawn) The method of claim 1, wherein said cells have an activity relating to the synthesis and/or the transport of GDP-fucose and/or to the activity of an enzyme involved in adding fucose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

7. (withdrawn) The method of claim 6, wherein the enzyme involved in the synthesis of GDP-fucose is selected from the group consisting of GMD (GDP-D-mannose 4,6-dehydratase), Fx (GDP-keto-6-deoximannose 3,5-epimerase, 4-reductase) and GFPP (GDP-beta-L-fucose pyrophosphorylase).

8. (withdrawn) The method of claim 6, wherein said enzyme involved in adding fucose is a fucosyl transferase.

9. (withdrawn) The method of claim 1, wherein, if in step b), the measured ratio is larger than 0.6, a defucosylation is performed and/or galactose residues are added to said antibody before step c).

10. (withdrawn) The method of claim 9, wherein said defucosylation is performed by adding a fucosidase in the medium containing the antibody.

11. (withdrawn) The method according to of claim 1, wherein the addition of galactose residues is performed by adding a galactosyl transferase in the medium containing the antibody.

12. (withdrawn) The method according of claim 1, wherein said cells stem from animal or human cell lines selected from the group consisting of rat myeloma YB2/0, rat myeloma IR983F, human myeloma Namalwa, cell of human origin, PERC6, CHO lines, CHO-K, CHO-Lec10, CHO-Lec1, CHO Pro-5, CHO dhfr-, CHO Lec13 lines, Wil-2, Jurkat, Vero, Molt-4, COS-7, 293-HEK, BHK, K6H6, NSO, SP2/0-Ag 14 and P3X63Ag8.653.

13. (withdrawn) The method of claim 1, wherein said antibody is an IgG type human immunoglobulin.

14. (withdrawn) The method of claim 1, wherein said antibody is selected from the group consisting of an anti-Rhesus factor (anti-D), anti-CD, anti-tumors, anti-virus, anti-CD20 and anti-HLA-DR.

15. (withdrawn) The method according of claim 1, wherein said effector activity is a ADCC type functional activity.

16. (withdrawn) A method for increasing the effector activity of a composition of immunologically functional molecules, comprising the increase in galactose content and/or reduction in fucose content of the composition of molecules.

17. (withdrawn) The method of claim 16, wherein said immunological functional molecules are monoclonal or polyclonal antibodies.

18. (withdrawn) The method of claim 16, wherein said molecules have high fucose content in the native condition.

19. (withdrawn) The method of claim 16, wherein the reduction in fucose content is due to a defucosylation of said composition through the action of a fucosidase.

20. (withdrawn) The method of claim 16, wherein the increase in galactose content of said composition is due to a galactosylation of the composition through the action of a galactosyl transferase.

21. (withdrawn) A cell derived from the YB2/0 cell line, in which at least one vector coding for an antibody molecule is introduced, said cell producing an antibody for which the fucose content/galactose content ratio of the

oligosaccharides of the glycosylation site of the Fc region of the antibodies is less than or equal to 0.6.

22. (withdrawn) The cell of claim 21, wherein said cell is transfected with an expression vector coding for a galactosyl transferase.

23. (withdrawn) The cell of claim 21, wherein said galactosyl transferase is a beta(1,4)-galactosyl transferase or a beta(1,3)-galactosyl transferase.

24. (withdrawn) The cell of claim 21, wherein said cell overexpresses said galactosyl transferase.

25. (withdrawn) The cell of claim 21, wherein said galactosyl transferase is coded by a sequence originating from humans, mice, hamsters, cows, sheep, goats, pigs, horses, rats, monkeys, rabbits or chickens.

26. (withdrawn) The cell of claim 25, wherein said sequence is the NM 001497, AB 024434, NM 003780, BC 053006, XM 242992, or NM 177512 sequence.

27. (withdrawn) A method for preparing antibodies for which the glycanic structures borne by the glycosylation site of the Fc region has a fucose content/galactose content ratio less than or equal to 0.6, comprising the culture of a cell of claim 21 in a culture medium and under conditions allowing expression of said vectors.

28. (currently amended) Therapeutic antibodies having high effector activity obtained from the method of claim 1, ~~wherein, said antibodies have on their glycosylation site of the Fc region, glycanic structures having a fucose content/galactose content ratio less than 0.6 comprising:~~

- a) producing and purifying monoclonal antibodies obtained from different sources selected from the

- group consisting of cells, plants and non-human animals,
- b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies, and
- c) selecting antibodies for which the fucose content/galactose content ratio is between 0.5 and 0.35.

29. (original) A pharmaceutical composition comprising an antibody according to claim 28 and at least one excipient.

30. (currently amended) A pharmaceutical composition comprising at least 50% of a monoclonal antibody for which the glycanic structures borne by the glycosylation site of the Fc region have a fucose content/galactose content ratio ~~less than 0.6~~ between 0.5 and 0.35.

31. (previously presented) The pharmaceutical composition of claim 29, wherein the antibody is directed against a non-ubiquitous normal antigen, or an antigen of a pathological cell or on a pathogenic organism for humans.

32. (previously presented) The pharmaceutical composition of claim 29, wherein said antibodies are IgGs.

33. (withdrawn) A method for treating allo-immunization, comprising administering the antibody of claim 28 to a patient in need thereof.

34. (withdrawn) A method for treating an auto-immune disease, a cancer or an infection by a pathogenic agent comprising administering the antibody of claim 28 to a patient in need thereof.

35. (withdrawn) A method for treating cancers of positive class II HLA cells, acute lymphoid leukemias of B- and T-cells, acute and chronic myeloid leukemias, Burkitt's lymphoma, Hodgkin's lymphoma, myeloid leukemias, T-cell lymphomas, and non-Hodgkinian lymphomas, comprising administering the antibody of claim 28 to a patient in need thereof.

36. (withdrawn) The method of claim 33, wherein said antibody is an anti-HLA-DR or an anti-CD20.

37. (withdrawn) A method for inducing expression of IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-12, IL-18, IL-21, TGF β 1, TGF β 2, TNF α , TNF β , IFB γ , or IP10 by natural effector cells of the immune system comprising administering the antibody of claim 28 to a patient in need thereof.

38. (withdrawn) A method for treating patients having one of the polymorphisms of CD16, in particular V/F158 or F/F158, notably patients in a condition of therapeutic failure with the presently available antibodies or subject to undesirable secondary effects comprising administering the antibody of claim 28 to a patient in need thereof.

39. (withdrawn) A method for preparing a human or humanized chimeric monoclonal antibody having low effector activity, comprising:

- a) producing and purifying monoclonal antibodies obtained from different sources selected from the group consisting of cells, plants, and non-human animals,
- b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies,
- c) selecting antibodies for which the fucose content/galactose content ratio is larger than 0.6.

40. (withdrawn) The method of claim 39, wherein said antibodies are produced in genetically modified cells by introducing at least one vector allowing expression of said

antibodies, said cells being eukaryotic or prokaryotic cells selected from the group consisting of cells from mammals, insects, plants, bacteria, or yeasts.

41. (withdrawn) The method according of claim 39, wherein said cells are genetically modified by introducing at least one vector allowing expression of at least one polypeptide having a glycosyl transferase activity.

42. (withdrawn) The method of claim 41 wherein said glycosyl transferase activity is a fucosyl transferase activity.

43. (withdrawn) The method according of claim 39, wherein said cells have an activity relating to the synthesis and/or the transport of UDP-galactose and/or to the activity of an enzyme involved in adding galactose to the oligosaccharide of the glycosylation site of the antibodies, either reduced or deleted.

44. (withdrawn) The method of claim 43, wherein said enzyme involved in the addition of galactose is a galactosyl transferase.

45. (withdrawn) The method of claim 39, wherein, if in step b), the measured ratio is less than 0.6, fucosylation is performed, and/or galactose residues are removed from said antibody before step c).

46. (withdrawn) The method of claim 45, wherein said degalactosylation is performed by adding a galactosidase in the medium containing the antibody.

47. (withdrawn) The method of claim 45, wherein addition of fucose residues is performed by adding a fucosyl transferase in the medium containing the antibody.

48. (withdrawn) The method of claim 39, wherein said antibody is an IgG type human immunoglobulin.

49. (withdrawn) The method of claim 39, wherein said antibody is directed against a CD, a differentiation marker of human blood cells or against a pathogenic agent or its toxins, listed as being particularly dangerous in the case of bioterrorism, selected from the group consisting of *Bacillus anthracis*, *Clostridium botulium*, *Yersinia pestis*, *Variola major*, *Francisella tularensis*, filoviruses, arenaviruses, *Brucella species*, *Clostridium perfringens*, *Salmonella*, *E.coli*, *Shigella*, *Coxiella burnetii*, ricin toxin, *Rickettsia*, viral encephalitis viruses, *Vibrio cholerae* and hantavirus.

50. (withdrawn) The method of claim 39, wherein said effector activity is an ADCC type functional activity.

51. (withdrawn) A method for reducing the activity of a composition of immunologically functional molecules, comprising the increase in the fucose content and/or the reduction in the galactose content of said composition.

52. (withdrawn) The method of claim 51, wherein said immunologically functional molecules are monoclonal or polyclonal antibodies.

53. (withdrawn) The method of claim 51, wherein the increase in the fucose content is due to fucosylation of said composition through the action of a fucosyl transferase.

54. (withdrawn) The method according of claim 51, wherein the reduction in the galactose content of said composition is due to degalactosylation of the composition through the action of a galactosidase.

55. (withdrawn) An antibody obtained from a method of claim 39.

56. (withdrawn) A method for treating and/or preventing auto-immune diseases, allo-immunizations, notably PTI, graft rejection, allergies, asthma, dermatites, urticarias, erythemas, or inflammatory diseases comprising administering the antibody of claim 55 to a patient in need thereof.

57. (withdrawn) A method for controlling the activity of a composition of immunologically functional molecules, comprising the regulation of the fucose content/galactose content ratio of the oligosaccharides of the glycosylation site of the Fc region of the antibodies.